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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,196	09/22/2000	Stephen James Russell	18093/1130	9873

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/668,196

Applicant(s)

RUSSELL ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,9,11-22,24,26 and 28-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9, 11-22, 24, 26, 28-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of the Claims

1. Claims 1-7, 9, 11-22, 24, 26, 28-33 are pending and under consideration in the present action. The claims were rejected in the action mailed on November 17, 2003. No amendments were made in the Response filed by applicant on February 20, 2004.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **(Prior Rejection- Maintained)** Claims 31 and 32 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims read on the use in a method to treat mammals with a cancer with attenuated Measles virus with point mutations in the genome. The Applicant traverses this argument of the basis that "A person having ordinary skill in the art at the time the Applicant's filed would have been able to obtain an attenuated measles virus containing point mutations." However, while the Examiner agrees that those in the art would be able to obtain attenuated

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measles virus without undue experimentation, such virus may or may not contain point mutations or non-sequential point mutations as required by the claims.

It is known in the art how to passage virus in order to achieve attenuated virus. However, such a mode of operation is not dependant on the type of mutation made to the viral genome. In order to make and use attenuated virus according to claims 31 and 32, those in the art would be required to first make a virus with specific point mutation, of which there are many thousand possible variations within the genome, and determine which of these is attenuated. There is no guidance in the application as to which of the many possible mutations would result in an attenuated virus. Further, as was described in the prior action, the effect of any particular point mutation on the viral activity is unpredictable. In view of the broad scope of the claims, the unpredictability of the affect of any particular point mutation, and the lack of guidance in the application, there is little evidence that those in the art would be able, without undue experimentation, to make attenuated virus with the specific types of mutations required by claims 31 and 32. Because the Applicant has provided no evidence to the contrary, the rejection is maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. **(Prior Rejection-Maintained)** Claims 1-7, 9, 11-17, 20-22, 24, and 28-33 were rejected in the prior action under 35 U.S.C. 103(a) as obvious over Bateman et al (Cancer Research 60:1492-1497- Bateman 2000) in view of Wiebel et al. (Arch. Dis. Childhood 48:532-536 1973), and further in light of the teachings and suggestions of Linardakis (Gene Therapy 6, supp 1, page S4, abstract 13), the Bateman abstract (Gene Therapy 6, supp 1, page S6, abstract 24), Taqi (The Lancet, May 16, 1981, page 1112), Bluming (The Lancet, July 10, 1971, pages 105-06), and Johnston (J Virol 73(8): 6903-15). The claims have been described in the prior action. The Applicant traverses this rejection on three general grounds.

The first argument in traversal, arguing that there are differences between the Bateman 2000 reference and the claimed invention, appear to be merely repeating earlier arguments presented by the Applicant, and responded to in the prior action. As indicated in the prior action, the fact that the Bateman 2000 reference has noted that the protocol for the test was different from that originally indicated does not teach change the conclusions drawn from the test. In addition, the argument is focused only on the differences between Bateman 2000 and the claimed methods, and does not consider the teachings of the additional references. Thus, the traversal is not found persuasive for the reasons indicated in the prior action.

The second argument presented by the Applicant is that the art does not suggest that use of an attenuated measles virus in a method to reduce the number of viable cancer cells in a subject. In particular, the Applicant challenges the applicability of the Bateman 2000 and the Weibel references as art against the claimed invention by asserting that the teachings of Bateman 2000 “falls far short of suggesting ... [the use of] an attenuated measles virus to reduce the number of viable cancer cells in a mammal”; and that Weibel “has nothing to do with viral

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vectors, the use of viral vectors, or the use of attenuated measles virus to reduce the number of cancer cells in a mammal.” The Examiner agrees both that Bateman 2000 alone does not suggest the claimed invention, and that the teachings of Weibel, in absence of additional teachings, provide no motivation to use the attenuated virus as a treatment for cancer. However, the shortcomings of individual references are not sufficient to overcome a rejection of claims based on a combination of references. See, In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); and In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Examiner does not agree that the combination of the cited references fails to teach the claimed invention.

The teachings of the prior art references have been described in the prior actions. As indicated, Bateman 2000 suggests the use of DNA encoding measles virus fusogenic membrane glycoproteins (FMGs) for the treatment of cancers in vivo. See e.g., pages 1495, and 1497. In addition to these teachings, the art both suggests the use of live viral vectors to deliver FMG DNA into cells (Bateman abstract, and Linardakis), and that the whole live measles virus is capable of causing regression of cancerous growths (Taqi and Bluming). In these references, the art indicates not only that genetic transformation of cancer cells with specific proteins of the measles virus can lead to cancer regression, but that such regression is also seen with infection by the whole virus; thereby indicating that the measles virus is itself an effective delivery vehicle for these anticancer proteins to the cells.

The Weibel reference further teaches the safety for human administration of an attenuated measles virus. While, as the Applicant points out, one of the two lines of attenuated measles virus may cause mild reactions, the reference in no way indicates that attenuated measles virus in general (or even the one indicated as causing mild reactions) was unacceptable for

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administration. In view of the teachings of the other references above, it would have been obvious to those in the art to substitute an attenuated measles virus, which would not result in the infections caused by a wild-type measles virus, for the wild-type virus which has been demonstrated to be effective in causing regression of tumors. The teachings of the Johnston reference, which indicates that the FMGs of the measles virus would be unaffected by the attenuation of the virus, illustrate that those in the art would have had a reasonable expectation of success in the use of the attenuated virus as carriers for the FMG particles. Thus, the art as a whole provides both suggestion and a reasonable expectation of success for the use of attenuated measles virus to reduce the number of viable cancer cells in a mammal. The Applicant's second argument is not found persuasive for the reasons above, and the reasons of record.

The Applicant's third argument in traversal of the rejection is that there is external evidence of the non-obviousness of the claimed invention. The Applicant argues both unexpected results of the claimed invention, and that the Applicant has satisfied a long-felt and recognized need in the art with the claimed invention. These arguments were addressed in the prior action. As no additional arguments have been presented, the rejection is maintained against these arguments for the reasons of record.

For the reasons above, and the reasons of record, the rejection of 1-7, 9, 11-17, 20-22, 24, and 28-33 over the teachings of Bateman 2000 in view of Weibel and further in light of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston is maintained.

6. **(Prior Rejection- Maintained)** The rejection of claims 1-7, 9, 11-22, 24, 26, and 28-33 was maintained in the prior action over the teachings of Bateman et al. in view of Usonis et al.

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(Ped Inf Dis J 18:42-48), and further in light of the teachings of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. For the reasons indicated above and in the prior actions, the rejection of claims 1-7, 9, 11-17, 20-22, 24, 26, and 28-33 is maintained over the teachings of Bateman et al. in view of Usonis, and further in light of the teachings and suggestions of Linardakis, the Bateman abstract, Taqi, and Bluming, and Johnston.

7. **(Prior Rejection- Maintained)** Claims 16 and 17 were rejected under 35 U.S.C. 103(a) as obvious over the teachings of Bateman et al. in view of either Weibel or Usonis, and in view of either Asada (Cancer 34: 1907-28, of record in the IDS filed on Jan 5, 2001) or Sato et al (Int J Oral Surg 8:205-11, of record in the IDS filed on July 12, 2002) and further in light of the teachings and suggestions of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. The claims and the teachings of the references other than Sato and Asada have been described above. The Applicant has presented no additional arguments in traversal of this rejection over those described above. The rejection is therefore maintained for the reasons indicated above.

8. **(Prior Rejection- Maintained)** The rejection of claims 18 and 19 is maintained for the reasons indicated above over the teachings of Bateman et al., in view of either Weibel or Usonis, further in view of Duprex (J Virol 73: 9568-75), and in light of the teachings of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. The rejection of these claims has been traversed for substantially the same reasons as, and is being maintained for the reasons indicated above with respect to, the rejections minus the Duprex reference above. While the Applicant is correct that the Duprex reference does not teach the use of the disclosed recombinant virus for the

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treatment of cancer, it would have been obvious to those in the art to incorporate the GFP marker into the attenuated virus for use as suggested such that the progress of the treatment could be measured.

9. **Prior Rejection- Maintained)** The rejection of claim 20 is maintained over the teachings of either Galanis et al. (Gene Therapy 6 (Supp 1): S7, abstract 28) or Russell et al. (Proc. Am Assoc Cancer Res 41: 259, abstract 1648) in view of either Wiebel or Usonis, and further in light of the teachings of Linardakis, the Bateman abstract, Taqi, Bluming, and Johnston. This was previously stated as the rejection of claim 20 over the teachings of either Galanis or Russell in view of either Weibel or Usonis, and further in view of Linardakis, the Bateman abstract, Taqi, and Bluming. The rejection was traversed for substantially the same reasons as the other rejections above, and is maintained for the reasons described above and in the prior actions.

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

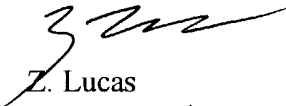
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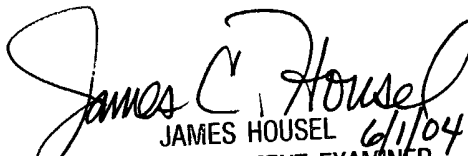
CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Z. Lucas
Patent Examiner


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